UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,747	08/25/1998	FERNAND NARBEY TOROSSIAN	TORO-0101-PU	8139

7590 12/12/2003

JOHN A ARTZ
LYON & ARTZ
28333 TELEGRAPH ROAD
SUITE 250
SOUTHFIELD, MI 48034

EXAMINER	
SHAHNAN SHAH, KHATOL S	
ART UNIT	**PAPER NUMBER**
1645	36

DATE MAILED: 12/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/125,747	Applicant(s) TOROSSIAN, FERNAND NARBEY	
	Examiner Khatol S Shahnan-Shah	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/14/03 and 10/1/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *36* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/1/2003 has been entered.

2. Applicant's amendment filed on 10/1/2003 has been entered. Claims 17-28 have been amended.

Status of The Claims

3. Claims 17-28 are pending. Claims 1-16 have been canceled.

Note: On 12/8/2003 the Examiner called attorney John A artz to clarify the status of claims 1-8. Claims 1-8 have been canceled via the amendment filed 6/26/2000.The amendment of 10/01/2003 listed those claims as withdrawn. The attorney agreed with the Examiner that indeed those claims were cancled not withdrawn (see interview summary, paper # 36).

4. Claims 17-28 are pending and under consideration.

Prior Citations of Title 35 Sections

5. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

6. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 or form PTO-1449 have submitted with this office action.

Objections Maintained

7. Objections to the specification made in paragraph 5 of the office action mailed April 08, 2002 (paper number 25) are maintained.

The objection was as state below:

The disclosure is objected to because of the following informalities:

Use of the brackets in the specification could lead to deletion of information within the brackets during the issue and printing processes. Accordingly, the portion of the specification as identified below is required to have the brackets removed before passing the case to issue. See 37 CFR 1.125 and MPEP § 608.01(q). For example the brackets are used in the specification page 1, (lines 8 and 11), page 3 (line 19), page 4 (line 1), page 6 (line 8), page 7 (line 11) and page 16 (lines 15, 19 and 22).

Applicant's response of 10/15/2002 has been noted that the square brackets will be removed at a later date. However the applicant has not submitted corrections so far.

Rejections Withdrawn

8. The rejection of claims 17-28 under 35 USC § 112, second Paragraph made in paragraph 12 of the office action mailed 2/17/2003 (paper number 28) is withdrawn in view of the applicant's amendments of the claims.

Rejections Maintained

9. The rejection of claims 17-28 under 35 USC § 112, first Paragraph made in paragraph 7 of the office action mailed April 08, 2002 (paper number 25) is maintained.

The rejection was as stated below:

Claims 17-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to an immunomodulatory and anti-*Helicobacter*- specific vaccine complex.

The specification fails to set forth sufficient evidence showing that the claimed vaccine complex could be made without undue experimentation. There is no evidence that subjects of Examples 2-4, who were treated with the complex of the instant invention, were effectively treated against Helicobacter- induced gastritis or duodenal ulcer, because there is no disclosure about the actual etiology of gastritis or duodenal ulcer in these subjects.

Claims recite the immunomodulatory and vaccine complex of the instant invention for use in the treatment of diseases caused by *Helicobacter* bacteria "by the production of antibodies". However, the specification on page 3, lines 3 and 4, states the "inefficacy" of the *Helicobacter*-specific antibodies in protecting an individual.

Furthermore, page 13 of the specification recites collagen type III as the "immunity adjuvant factor", and the complex as containing "amino acid sequences" of the collagen type III. However, claims 11 and new claim 18 recite that the amino acids from collagen are selected from the various amino acids recited in the claims. The collagen type III is stated on page 13 to be characterized by "Amino acid sequences containing the following concentrations expressed in g/kg" shown on page 13, wherein several individual amino acid residues are recited one below the other. No amino acid sequences are provided or identified specifically by a SEQ ID number. It is unclear what Applicant means by "amino acid

sequences" from collagen to the individual amino acids concentrations in g/kg (not sequences) recited on page 13. With this description, one of ordinary skill in the art would not be able to understand whether the whole sequence is present in the complex, or any one of the recited amino acids is included in the complex, or a mixture of any of these amino acids is included in the complex, and therefore would not be able to make and/or use and/or reproducibly practice the invention without undue experimentation.

Further, the specification does not allow one of ordinary skill in the art to grasp the nature of the association between the multiple components present in the "complex". For example, the optimal amounts or proportions of different "bacterial membrane fractions", i.e., glycopeptides and/or lipopolysaccharides and the ribonucleic acid arm, that should be present in the complex such that the complex can accomplish its alleged therapeutic and/or preventive functions are not disclosed.

The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity for prevention or treatment of *Helicobacter* infection. The art recognized standard for the determination of *Helicobacter pylori* infection is endoscopy and evaluation of tissue samples for the presence or absence of *Helicobacter* (see page 661, Buck et al, 1986). Data obtained from challenge experiments must demonstrate an art recognized standard of improvement over the control in order for the composition to be considered as being useful for treatment or prevention of infection and disease. This information is essential for the skilled artisan to be able to use the claimed composition (vaccines) for their intended purpose of a *Helicobacter* vaccine. Without this demonstration, the skilled artisan would not be able to

reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

The prior art teaches that *Helicobacter pylori* vaccines are unpredictable, specifically, in the type of effect they will have on preventing or treating infection; the ability to reasonably predict the capacity of a single bacterial immunogen, to induce protective immunity is problematic. In HP WORLD-WIDE, a publication from Brocades Pharma BV Leiderdorp, The Netherlands, February 1992, data was presented stating that immunization does not appear promising. Parenteral immunization of specific pathogen free mice with *H. felis* gave no protection against gastric colonization; previous oral infection only delayed colonization (page 3, Heap, K, Australia). The article also taught that "although intra-peyers patch immunization of killed *H. pylori* in rats shows that the gut mucosa can mount a vigorous immune response, oral immunization with either live or killed bacteria induced no significant serum or salival antibody response (page 3 Dunkley, M, Australia). Blaser also warned that because of the possible autoimmune component of the disease the wrong vaccine could actually make things worse." (see page 3).

Yokota et al (1997) teaches that *Helicobacter pylori* polysaccharide are of low antigenicity and that while some strains stimulated an immune response *in vivo*, it was strain specific (see abstract and page 3509).

It is known in the art that vaccines convey protection from infection and disease. Rappuoli et al (European Journal of Gastroenterology and Hepatology, 1993, Vol.5, (suppl. 2) pages 576-578) teach that development of a vaccine against *Helicobacter pylori* would involve four major steps:

1) identification of the factors required for virulence;

2) large-scale production and characterization of the virulence factors;

3) development of appropriate animal models to test the virulence and immunogenicity of the molecules identified; and

4) identification of the type of immunity able to prevent infection and disease (see abstract).

In the instant specification no art recognized *in vitro* or *in vivo* models are shown in which protection is produced from instantly claimed invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the court of appeals in In re Wands, 8 USPQ 2d 1400 at 1404 (CAFC 1988).

These factors include 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, and 8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to a vaccine complex having claimed functional feature of capability of generating protective responses, 3) there are no working examples which suggest the desired results of a vaccine against *Helicobacter*, 4) the nature of the invention involved the complex and incompletely understood area of protective immune responses against *Helicobacter*, 5) the state of the prior art shows the lack of correlates to immunity with *Helicobacter*, 6) the relative

skill of those in the art is commonly recognized as quite high (post – doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, and lack of guidance on how to obtain the desired effect using the claimed vaccine complex it is determined that it would require undue experimentation to make and/or use the claimed invention. In summary, the actual invention is not described in such a way that one skilled in the art could grasp the invention and make and/or use the invention and/or reproducibly practice the invention with a reasonable expectation of success, without undue experimentation. In the absence of specific guidance and evidence, instant claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph.

Applicant's arguments filed 6/13/2003 have been fully considered but they are not persuasive.

Applicant argue, " The Examiner contends that the examples set forth in the specification (pages 22-24). Are insufficient to show that the claimed vaccine complex could be effective in "treating or preventing" disease or " how it can be made". In response, the Examiner is advised the " prevention" of disease is not an object of the invention and the specification is only directed to treatment of the anti-bio- resistant strain. Thus any data regarding "prevention" is unnecessary". Applicant further argue, " The process for producing the vaccine complex is similar to that described in the applicant's recently issued U.S. Patent No. 6,503,512 (apart from *Helicobacter*). It is submitted tat since the U.S. '512 patent has a similar type of disclosure as the

present application and was allowed by the Patent Office, that it would be inconsistent to maintain the 112 objection in this case".

It is the examiner's position that applicant claims a "vaccine complex" not a composition for treatment of antibiotic resistant *Helicobacter pylori*. In the instant case claims 17-28 are drawn to a vaccine. When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated base on that limitation. See in re Vaeck, 947 F. 2d 488, 495,20 USPQ 2d 1438, 1444 (Fed Cir, 1991).

Dorland's Medical Dictionary (29th Edition, 2000) defines "vaccine" as "a suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), or of antigenic proteins derived from them, administered for the prevention, amelioration, or treatment of infectious diseases. The applicant admits that " prevention" of disease is not an object of the invention and the specification is only directed to treatment of the anti-bio- resistant strain. However, the applicant claims recite a vaccine. In the instant case the applicant's invention is not enabled for the prevention of infectious diseases.

It is the examiner's position that applicant argument in regard to U.S. Patent No. 6,503,512 is not persuasive. Because the claims of U.S. Patent No. 6,503,512 is not drawn to a vaccine.

If the applicant believes that a telephonic or a personal interview would help to clarify these issues the office will these issues, the examiner would try to arrange an interview upon applicant's request.

Conclusion

10. Claims 17-28 stand rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-

8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

December 10, 2003

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER